

### **REMARKS/ARGUMENTS**

Claims 1–9 are pending and under examination in the captioned application. The specification has been amended. The claims have been amended. Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments. Applicants respectfully submit that the amendments are fairly based on the specification and respectfully request their entry.

#### **Specification Objections**

The Examiner has objected to two informalities in the specification. First, the Examiner again objected to the use of trademarks, specifically the improper use of the trademarks PCR<sup>TM</sup> and TRIS<sup>®</sup> and suggested an acceptable term for “Tris.HCl” as “TRIS<sup>®</sup> HCL (hydroxymethyl) aminomethane hydrochloride.” Applicants have amended the specification to fulfill the requirements of the Examiner.

Secondly, the Examiner has objected to the specification because the status of the priority document has not been updated. In response, Applicants have amended the first paragraph of the application first introduced in the preliminary amendment of January 14, 2004 to indicate that the United States patent application number 09/967,301, of which the instant application is a divisional, has been patented. However, Applicants submit that an Issue Notification has yet to be received and therefore do not know the assigned patent

number. Applicants will amend the specification again immediately upon receipt of the Issue Notification for the parent application.

Applicants respectfully submit that these amendments are fully supported by the specification and do not add new matter. Applicants request that the objections to the specification be withdrawn.

### **Claim Objections**

The Examiner has objected to claims 8 and 9 and suggested that the claims be amended to recite “A fluorescent protein” instead of “The fluorescent protein”. In response, Applicants have amended the claims to comply. Applicants request that the objections to the claims be withdrawn.

### **Claim Rejections – 35 U.S.C. § 101**

The Examiner has rejected claims 8 and 9. The Examiner states that “the claimed invention is directed to non-statutory subject matter”. Applicants respectfully disagree. Nonetheless, solely to expedite prosecution, Applicants have amended claims 8 and 9 by incorporating the Examiner’s suggestion. Both claims now recite “an amino acid sequence which is modified”, as claim 1. As such, Applicants respectfully submit that the rejection be withdrawn.

**Claim Rejections – 35 U.S.C. § 112**

The Examiner has rejected claims 1-7 “under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention.”

The sole issue here is whether or not the specification is enabling for any functional analogue. Applicants respectfully assert that the specification is enabling for GFP analogues containing the amino acid substitutions at the specified positions as claimed. Nonetheless, solely to expedite prosecution, Applicants have amended claim 1 by incorporating the Examiner’s suggestion. Therefore, the rejection has been obviated. Applicants respectfully request that the rejection be withdrawn.

**Claim Rejections – 35 U.S.C. § 112**

The Examiner has rejected claims 1, 3, 5 and 7, under 35 U.S.C. § 102(e), as being anticipated by Tsein et al. (U.S. 6,780,975). The Examiner states, “Tsein et al. teach modified GFPs having substitution at position F64, S65, E222 and S175 having different spectral properties than the wildtype GFP (claim 1, see SEQ ID NO:4 of the patent attached herein). The sequence disclosed by Tsein et al. has the Gly at position 175 (claim 3) and Leu at position 222 (claim 5), see SEQ ID NO:4. The modifications disclosed in the Tsein et al. patent are compared to the GFP wildtype protein, thus claim

7 is also anticipated (see SEQ ID NO:4 of the patent). Therefore, the limitations of the claims are met by the reference.”

In response, Applicants respectfully submit that Tsein et al. do not teach modified GFP having substitution at position F64, S65, E222 and S175. Applicants submit that SEQ ID NO: 4 of Tsein et al. does not teach such a modified GFP. In fact, according to Tsein et al., SEQ ID NO: 4 is that “of the engineered *Aequorea*-related fluorescent protein S65G/S72A/T203Y utilizing preferred mammalian codons and optimal Kozak sequence” (see column 2, lines 52-55). To generate SEQ ID NO:4, Tsein et al. added an Val(V2) between the first (Met) and second (Ser) amino acid sequence of the wildtype GFP sequence. Because of the addition of V2, the numbering of each of the subsequent amino acids of SEQ ID NO: 4 is shifted one from the wildtype sequence. As such, the positions where amino acid sequence substitutions occur in claim 1 of the instant application (F64, S65, E222 and S175) appear as F65, G66, E223 and S176 in SEQ ID NO: 4 of Tsein et al. The only amino acid sequence in Tsein et al. that changed from the wildtype sequence is S65G. Therefore, the rejection of claims 1, 3, 5, 7 under 35 U.S.C. § 102(b) should be withdrawn.

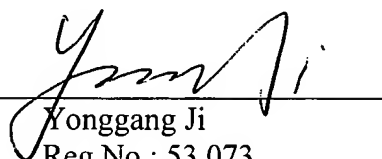
Applicants believe that the foregoing constitutes a full and complete response to all outstanding objections and rejections. Applicants further believe that this application is now in condition for allowance. However, should any issues remain, the Examiner is

respectfully requested to telephone the undersigned at (732) 908-2875 so that the issues might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,


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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on June 21, 2005.

Signature:   
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